

PROF. DR. FELIX HAUROWITZ

ISTANBUL UNIVERSITESI

ISTANBUL

Istanbul, February 10th, 1948

MH 32 D6

Professor Michael Heidelberger
Department of Biochemistry
Columbia University
620 West 168 Street
New York City

Dear Professor Heidelberger,

under the same cover I am sending you the copy of a short typescript returned to me by the "Archives of Biochemistry" and a copy of the referee's unfavourable comment. I am applying to you, because the referee bases his opinion on your work and because I am not able to understand what the referee means. I should be very much indebted to you for your authoritative interpretation of your own work.

I will admit, first of all, that I am ^{blamed} quite correctly for not having quoted your paper on serum albumin. I shall certainly correct this mistake. In the same paper you had shown, that anti-ovalbumin is not precipitated by azo-ovalbumin, so that you could not recommend your method as a method for the determination of antibodies. You attributed, at that time, precipitation or non-precipitation by azo-proteins to a property of the respective protein. Later I have shown that the main factor is the amount of azo-groups per protein molecule (J. Immun. 40, 392 (Table II) and that anti-ovalbumin is precipitated by azo-ovalbumin (ibid. 43, 333, Table 2). Therefore I am proposing now to determine antibodies against proteins by precipitation with azo-proteins poor in azo-groups. I believe that this idea is worth of a publication, and I think that 2 pages of a typescript are not exaggerated for the treatment of this problem.

The main point is however the assertion of the referee that it is unnecessary to resort to the "subterfuge" of azoproteins. Why? I have read very attentively the papers of your laboratory, quoted by the referee, and other papers of this series, but I really have no idea, what the referee means. Is there any other possibility of determining anti-globulins? The referee might have in mind your paper on thyroglobulin, where you have shown that all of the added antigen is precipitated as long as antibody is in excess, and that antibody can be calculated simply by subtraction of added antigen from total precipitate. But in other papers, on azo-ovalbumin, azo-serumalbumin, azo-streptoprotein, you have found that such a calculation is not valid, because a part only of the added antigen is precipitated. Now, there is one thing, which I could not understand, and which might have led the referee to the believe that such a simple calculation is possible in general; that is your similar assumption in other and even in your last papers (e.g. J. Am. Chem. Soc. 67, 585, 1945). In all of these papers you assume that all of the added antigen is precipitated. I have not been able to find any prove for this your opinion and I fear that I must have overlooked some important paper. In an older paper (J. exp. Med. 62, 697, 1935) you mention some of your reasons, among them the uniformity of ovalbumin. Since that time it has been proved that crystalline ovalbumin is not uniform; it is very well understandable, therefore, that a part might remain dissolved. My own experiments have led me to the opinion that not all of the added antigen is precipitated by antibody, even if the latter is in excess. Accordingly I see no other way to determine antibodies than by using labeled antigens, for instance azo-proteins, as shown in my paper. If I am mistaken, please correct me and, if you should understand the referee's opinion, please try to explain it to me. - The last sentence of the referee's comment is quite incomprehensible to me. If you could guess, what modification is meant, please explain it to me.

I am very sorry that my letter will cause you much work. But, please, do answer to me. The matter is of the utmost importance ~~MM~~ to me for two

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to Professor Heidelberger

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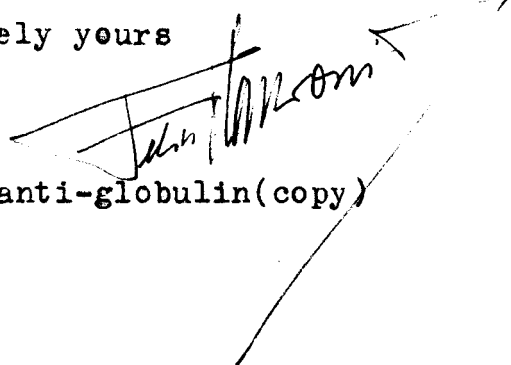
reasons. One of them is, that a similar thing happened two years ago with a paper sent to the J. Am. Chem. Soc. This paper also was returned to me with reference to your work. If this practice continues, the editors must get the impression that I am sending to them worthless papers. You can imagine that this will have tragic consequences for me in future.

The second reason for my applying to you directly is, however, the fact that both referees seem to assume that I disregard intentionally your results. This is particularly painful for me, because among all my American colleagues it has been just you who helped me most during the war time. Please believe me that it is far from me to disregard anything of your work. It is hardly possible to quote all pertinent papers in a short experimental paper. But I am very willing to send you my papers before submitting them to an editor, to prevent the omission of any important contribution of your laboratory.-

I would be very grateful to you, dear Professor Heidelberger, if you could help me in this matter by explaining to me the meaning of the comment of the referee, by informing me, what modification might have been wanted (last sentence of comment) and by explaining to me also the reason for your assumption, that all of the added antigen is precipitated, although you have proved the contrary in at least three antigens. I think that no differences can arise, if these questions are elucidated and I hope that you will be so kind as to help me to elucidate them.

Since common mail to Turkey takes 6 to 10 weeks, please use airmail for your answer. Neither the paper, nor the comment are required by me, since I have copies of both. With my kindest regards and best thanks.

Sincerely yours



Enclosed: typescript on determination of anti-globulin (copy)
comment of referee (copy)